AMENDMENTS TO THE SPECIFICATION

Please amend pages 8 and 9 of the specification to read as follows:

Figure 4A demonstrates that increasing concentrations of dominant negative forms of the aPKCs, ζPKC-DN and λ/tPKC-DN, are capable of inhibiting PS-1 induced NF-κB transcription activation. However ζPKC-DN inhibited signaling to a much greater extent and at lower concentrations. These data indicate that PSI induced NF-κB activation is mediated by ζPKC.

Figure 4B shows that exogenous ζPKC can rescue 293 cells from apoptotic cell death. The figure also demonstrates that ζPKC can rescue increased vunerability to apoptosis resulting from FAD PSI expression.

Figure 4C shows that Par-4 severely abrogates PSI induced NF-κB activation in 293 human embryonic kidney cells.

Figure 4D demonstrates that Par-4 inhibits PSI induced NF- B activation through the aPKCs. In the presence of an activated ζPKC mutant, Par-4 showed a significantly reduced ability to inhibit PSI mediated NF-κB activation.

Figure 4E demonstrates that PS-1 mediated NF-κB activation requires p62 activity. Overexpression of p62 increases the activation of NF-κB by PSI compared to control levels while expression of an anti-sense p62 construct reduces activation of NF-κB by PS 1 to levels below those seen when PS 1 VT is transfected alone.

Figure 5A, upper panel, illustrates that RIP co-immunoprecipitates with PSI in a TNFα dependent manner, indicating that PSI is involved in TNFα -induced NF-κB activation. The lower panel shows that the association between PSI and RIP temporally coincides with activation of NF-κB following stimulation with TNFα as determined by electrophoretic mobility shift assay.

Figure 5B indicates that PS1-WT has a synergistic effect on TNFα induced NF-κB activation.

Figure 5C indicates that like wild type PSI, PS1-FAD mutants synergistically increase TNFα induced NF-κB activation.

Figure 5D shows a bar graph indicating relative luciferase activity induced by PS1, PS1+TNFα, E280G, and E280G+TNFα.

Figure 6A demonstrates that TNFα treatment enhances the association between PS1 and RIP.

Figure 6B shows the results of electrophoretic mobility shift assays indicating that sequence specific NF-κB binding is transiently and maximally enhanced within 10 minutes of treatment with TNFα, thus correlating the association between PS1 and RIP demonstrated in Figure 6a with TNFα stimulation.

Figure 6C shows the results of an electrophoretic mobility shift assay.

Figure 7A shows quantitative RT-PCR analysis of Par-4 expression in PC12 cells stably expressing PC1-WT and PS1-FAD mutants following induction of apoptosis. Par-4 mRNA levels increased to a greater extent in the cells expressing PS1-FAD mutants.

Figure 7B shows that consistent with the results presented in Figure 7A, Par-4 protein levels are increased more rapidly and to higher levels in cells expressing PS1-FAD mutant protein when exposed to an apoptotic stimulus.

Figure 7C shows Par-4 protein levels produced over time.

Figure 8 shows NF-κB activation following an apoptotic insult in PC12 cells stably expressing PS 1 -WT or PS1-FAD. PS1-FAD expressing cells showed a significant reduction in specific NF-κB binding complex formation following etoposide treatment.

Figure 9A shows that the expression of a constitutively active ζPKC mutant can prevent the increased susceptibility to apoptosis seen in cells transiently transfected with PSI -FAD mutations.

Figure 9B shows that the expression of a constitutively active ζPKC mutant can prevent the increased susceptibility to apoptosis seen in PC12 cells stably expressing PS 1 -FAD mutations. This suggests that the increased susceptibility to apoptosis seen in these mutants may require inhibition of aPKC activity.

~~demonstrate that PS-1 induced NF- KB activation is mediated by @PKC.~~

Figure 10 is a chart illustrating the activation of NF-κB by the atypical protein kinases.

Figure 11A shows the nucleotide sequence encoding a human Par-4 protein (SEQ. ID NO: 1).

Figure 11B shows the deduced amino acid sequence of a human Par-4 protein (SEQ 10 NO: 2).

Figure 12A shows the nucleotide sequence encoding a human PS1 protein (SEQ. ID NO: 3).

Figure 12B shows the deduced amino acid sequence of a human PS1 protein (SEQ ID NO: 4).